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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,609	02/21/2002	Stefan Kochanek	50125/020002	7269

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/079,609	KOCHANEK ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7,8,11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 21-24* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-25 are pending.

Applicant's traversal and the amendment to claims 1, 9, 10 and 25 in paper filed on 8/2/06 is acknowledged and considered by the examiner.

Election/Restrictions

Claims 7, 8, and 11-20 and an anti-angiogenetic factor, anti-oxidative factor, lysosomal factor, vasodilating factor in claim 3 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and GDNF, NGF, BDNF, CNTF, bFGF and neurotrophin 3, 4-5 in claim 3 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/20/03.

Information Disclosure Statement

Applicant's request that examiner consider and initial the IDS mailed on 10/16/02. An IDS was not filed 10/16/02, but there was an IDS filed on 10/21/02. The IDS filed on 10/21/02 was already initialed and considered by the examiner. During a telephonic interview with applicant's representative on 10/31/05, the representative acknowledged that the IDS filed on 10/21/02 was the IDS mailed by applicant on 10/16/02. See interview summary 10/31/05.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 9, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi (US 2003/0045498) taken with Morsy et al. (PNAS, Vol. 95, 7866-7871, 1998).

Instant claims 1-6 and 21-24 are directed to product claims and the intended use of the product does not have patentable weight under a prior art rejection. See MPEP 2111.02.

Kovesdi teaches administering an adenoviral vector comprising a nucleic acid sequence encoding a pigment epithelium-derived factor (PEDF) to retinal pigment epithelial cells (abstract, pages 2, 3, 4, 6, 15, and 16). Kovesdi teaches that the adenoviral vector is deficient in genes essential for viral replication such that the vector can accept large inserts of exogenous DNA (pages 4-5). Kovesdi teaches that any promoter can be used in the vector, e.g., constitutive, regulatable, tissue-specific (pages 6-7). Kovesdi teaches a pharmaceutical composition comprising the vector and using the vector to study treatment of ocular disorders

(pages 12 and 13). However, Kovesdi does not specifically teach using a gutless adenoviral containing no adenoviral coding DNA sequences and no E. Coli coding DNA sequences.

However, at the time the invention was made, a HD adenoviral vector (also known as gutless adenoviral vector) comprising an exogenous gene was readily available for use to one of ordinary skill in the art as exemplified by Morsy (page 7866). Morsy teaches that "These HD vectors have up to 37 kb insert capacity, are easily propagated in a Cre recombinase-based system, and can be produced to high concentration and purity (>99.9% helper-free vector" (abstract). Morsy teaches that, "The greater safety, efficient gene delivery, and increased insert capacity of HD vectors are significant improvements over current Ad vectors and represent favorable features especially for clinical gene therapy applications" (abstract).

Accordingly, in view of the prior art represented by Kovesdi taken with Morsy, one of ordinary skill in the art would have had sufficient motivation to produce genetically modified RPE comprising recombinant HD adenoviruses with a reasonable expectation of success.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Morsy to produce a genetically modified pigment epithelial cell comprising an adenoviral vector comprising a nucleic acid encoding PEDF operatively linked to a promoter, wherein the vector comprises neither adenoviral coding DNA sequence nor E. coli DNA. One of ordinary skill in the art would have been motivated to produce the cell to study the treatment of ocular disorders by expressing PEDF in cells. In addition, one ordinary skill in the art would have been motivated to use gutless adenoviral vectors instead of the adenoviral vector taught by Kovesdi for producing the cell because one of ordinary skill in the art can insert large DNA coding sequences into the

gutless vectors. In addition, the gutless adenoviral vector taught by Morsy is readily available to one of ordinary skill in the art. Furthermore, the vectors have reduced immunogenicity compared to adenoviral vector having adenoviral DNA coding sequence because it does not contain adenoviral coding DNA sequences and would result in an increase in PEDF expression in the cell because the immune response would not interfere with the gutless adenoviral vector before the gutless adenoviral vector transfects the cell and expresses the PEDF.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Morsy to genetically modify pigment epithelial cell with an adenoviral vector comprising a nucleic acid encoding PEDF operatively linked to a promoter, wherein the vector comprises neither adenoviral coding DNA sequence nor E. coli DNA. One of ordinary skill in the art would have been motivated to produce the cell to study the treatment of ocular disorders by expressing PEDF in cells. In addition, one ordinary skill in the art would have been motivated to use gutless adenoviral vectors instead of the adenoviral vector taught by Kovesdi for producing the cell because one of ordinary skill in the art can insert large DNA coding sequences into the gutless vectors. In addition, the gutless adenoviral vector taught by Morsy is readily available to one of ordinary skill in the art.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 7-11, filed 8/2/06, with respect to the rejection(s) of claim(s) under 103(a) over Reichel or Reichel et al. further in view of Kovesdi have been fully considered and are persuasive. Therefore, the rejection has been withdrawn because of the

amendment to the claims. However, upon further consideration, a new ground(s) of rejection is made in view of Morsy et al. (PNAS, Vol. 95, 7866-7871, 1998).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi (US 2003/0045498) taken with Morsy et al. (PNAS, Vol. 95, 7866-7871, 1998) as applied to claims 1-6, 9, 21-24 above, and further in view of Tezel et al., (Exp. Eye Res. (1998) 66, 807-815).

Kovesdi taken with Morsy do not specifically teach culturing the genetically modified retinal pigment epithelial cell (RPE) of the eye in serum-free media.

However, at the time the invention was made, Tezel teaches that serum-free media can be used for culturing RPE cells (page 807). Tezel further teaches culturing the cells onto tissue-culture plastic pre-coated with bovine corneal endothelial extracellular matrix (page 807). Tezel teaches, "The presence or absence of serum-derived hormones, cytokines, carrier proteins, cell attachment factors and cell spreading factors can have a profound effect on the behavior of RPE cells in tissue culture and may mask the specific effects of a particular exogenous cytokine(s) on RPE. For these reasons, several researchers have cultured RPE with reduced or not serum supplementation (page 807)." Tezel teaches, "This is particularly important for RPE, because RPE cells exhibit phenotypic heterogeneity (page 812)."

Accordingly, in view of the prior art represented by Kovesdi taken with Morsy in further view of Tezel, one of ordinary skill in the art would have had sufficient motivation to produce genetically modified RPE comprising recombinant HD adenoviruses with a reasonable expectation of success.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kovesdi taken with Morsy in further view of Tezel to culture genetically modified retinal pigment epithelial cells in serum-free media. One of ordinary skill in the art would have been motivated to culture the RPE cells in serum-free media because Tezel teaches that culturing RPE cells in serum-free medium avoids the effect of hormone, cytokines, carrier proteins, cell attachment factors and cell spreading factors on the behavior of RPE cells in tissue culture.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claim 10 have been considered but are moot in view of the new ground(s) of rejection.

Response to Arguments

Applicant's arguments, see pages 7-11, filed 8/2/06, with respect to 103(a) over Reichel, Funk and Williams have been fully considered and are persuasive. The rejection of claim 25 has been withdrawn because RPE cells are not considered progenitors cells as taught by Funk (column 17, lines 8-11).

Conclusion

Instant claim 25 is free of the prior art of record.

Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman